



Postoperative treatment in margin positive patients of non-small cell lung cancer

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The treatment of non-small cell lung cancer varies in local treatment and general treatment. Surgery and radiation are representative strategies of local treatment, while general therapy is conducted choosing cytotoxic agents, molecular targeted agents and immune checkpoint inhibitors. Among local treatment, surgery can most frequently achieve complete removal of cancer lesion, thus the priority is the first to treat patients with NSCLC with limited status. Even among patients with stage IA NSCLC, cancer recurrence occurs in approximately 20% patients who underwent complete resection (R0) (1). These recurrences rise from residual isolated tumor cells (ITCs) underlying in niches of the region, the local and the distant place (2,3), thus the provability of recurrence depends on the tumorigenesis of ITCs (3), the potential of which could be indicated by the morphology of circulating tumor cells (CTCs) surrogating the existing ITCs; cluster CTCs represent extremely higher potential of metastasis than single CTC does (4). The prevalence of cluster CTC associated with the cancer stage (5), thus the potential of recurrence is high in the advanced stage NSCLC. In contrast, the prevalence of single CTC associates with early stage NSCLC and small tumor size and invasiveness (6), thus it is speculated that efficacy of adjuvant treatment is not high in stage IA NSCLC.

Recently Smeltzer *et al.* report on survival impact of

postoperative therapy modalities according to margin status in NSCLC using National Cancer Database (NCDB) in United States referring National Comprehensive Cancer Network (NCCN) (7,8), resulting in that mono-modality postoperative radiotherapy was not validated for any stage, although specific studies are needed to determine optimal management after incomplete resection. The Smeltzer's comprehension of adjuvant treatment for patients of incompletely resected NSCLC is shown in *Table 1*. In the analyses using whole cases of NCDB, radiotherapy alone may not effective but validated in stage IA patients which are recommended in NCCN guidelines. Besides they argued that NCCN adjuvant therapy guidelines after complete resection, based on high-level evidence, are validated, but not guidelines for patients with incompletely resected early-stage NSCLC, which are based on low-level evidence.

In surgical patients with NSCLC, incomplete resection is not frequent, but the prognosis is poor, thus proper treatment strategy is necessary to improve the outcome. Not to mention, it is crucial to make high quality observation using a data of great number of patients with incompletely resected NSCLC accompanying additional tumorigenic information of residual tumor cells which is able to take from observation on CTCs and ITCs as well as tumor pathology.

Table 1 Adjuvant therapy in stage IA–IIIA NSCLC recommended by NCCN and NCDB

NCCN group	Stage (T, N status)	Margin status	NCCN	NCDB	
				Whole	Adjusted
Group 1	IA (T1ab, 0)	Negative	O	O	O
		Positive	RTx	O	RTx
Group 2	IB (T2a, N0)	Negative	O or CTx	CTx	RTx +/- CTx
	IIA (T2b, N0)	Positive	RTx +/- CTx	CTx	CTx
Group 3	IIA (T1ab–T2a, N1)	Negative	CTx	CTx	–
	IIB (T3, N0; T2b, N1)	Positive	CTx + RTx	CTx +/- RTx	CTx or RTx
Group 4	IIIA (T1-3, N2; T3, N1)	Negative	–	–	CTx +/- RTx
		Non-N2	CTx	CTx	–
		N2	CTx + RTx	CTx +/- RTx	–
		Positive	CTx + RTx	CTx + RTx	CTx +/- RTx

NSCLC, non-small cell lung cancer; O, observe; NCCN, National Comprehensive Cancer Network; NCDB, National Cancer Database; RTx; radiation therapy, CTx, chemotherapy.

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References

1. Sawabata N, Miyaoka E, Asamura H, et al. Japanese lung cancer registry study of 11,663 surgical cases in 2004: demographic and prognosis changes over decade. *J Thorac Oncol* 2011;6:1229-35.
2. Bottos A, Hynes NE. Cancer: Staying together on the road to metastasis. *Nature* 2014;514:309-10.
3. Aceto N, Bardia A, Miyamoto DT, et al. Circulating tumor cell clusters are oligoclonal precursors of breast cancer metastasis. *Cell* 2014;158:1110-22.
4. Yu M, Bardia A, Wittner BS, et al. Circulating breast tumor cells exhibit dynamic changes in epithelial and mesenchymal composition. *Science* 2013;339:580-4.
5. Funaki S, Sawabata N, Nakagiri T, et al. Novel approach for detection of isolated tumor cells in pulmonary vein using negative selection method: morphological classification and clinical implications. *Eur J Cardiothorac Surg* 2011;40:322-7.
6. Tanaka F, Yoneda K, Kondo N, et al. Circulating tumor cell as a diagnostic marker in primary lung cancer. *Clin Cancer Res* 2009;15:6980-6.
7. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer NCCN guidelines Version 3. 2018.

Available online: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf, accessed February 23, 2014.

8. Smeltzer MP, Lin CC, Kong FS, et al. Survival impact

of postoperative therapy modalities according to margin status in non-small cell lung cancer patients in the United States. *J Thorac Cardiovasc Surg* 2017;154:661-672.e10.

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